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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/594,839 | 06/15/2000 | James Anthony | 2629-4017 | 3097 |

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| EXAMINER | |
|---|---|
| CHUNDURU, SURYAPRABHA | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

DATE MAILED: 04/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/594,839 | ANTHONY ET AL. | |
| | Examiner | Art Unit | |
| | Suryaprabha Chunduru | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-46 and 48-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46 and 48-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



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## DETAILED ACTION

1. Applicants' response to the office action filed on 2/15/05 has been entered.

2. Claims 1-46 and 48-55 are pending.

### Response to arguments

3. Applicants' response to the office action is fully considered and found not persuasive. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL.

4. The following is the rejection made in the previous office action:

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-46, 48-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Impraim et al. (USPN. 6,228,578) in view of Nathan et al. (USPN. 6,057,099) and Shah et al. (USPN. 5,629,156).

Impraim et al teach a method of claims 1, 22, 37-38, and 40, 46, of detecting a target nucleic acid comprising:

(a) hybridizing a target nucleic acid sample with probes (which include a mixture of HPV 6 and HPV 11 probes which are considered as capture and signal probes, biotinylated or enzyme labeled) hybridizing to said target nucleic acid at different regions (non-overlapping regions) to a to form a double-stranded hybrids (see column 6, line 34-40, col. 7, line 5-10);

(b) adding a blocker to the hybridization reaction, where in said blocker hybridizes to excess non-hybridized probe sequences (see column 9, line 20-50);

(c ) capturing the sequence probe:target hybrid to form a bound hybrid (see col. 7, line 14-22);

(d) detecting the bound hybrid (see column 9, line 51-67).

With regard to claims 3, 5, 24-26, 43-44, Impraim et al. teach that the capture probe is modified with a biotin ligand (see col. 6, line 43-47);

With regard to claims 11, 30, Impraim et al teach that the method comprises forming single stranded DNA (denature DNA) prior to hybridization (see co. 17, lines 25-29);

With regard to claim 14, 39, Impraim et al. teach that the blocker probe has lower melting temperature than that of capture sequence probe (see col. 9, line 20-37);

With regard to claim 15-18, 23, 32-35, 41, Impraim et al. teach immobilization of probe-target hybrid to streptavidin coated tubes or microtiter plates (see col. 7, line 47-67, col. 8, line 1-39);

With regard to claims 10, 19-20, 21, 22, 36, 42, Impraim et al. also teach that detection of bound hybrid using antibody wherein the hybrid is labeled with alkaline phosphatase enzyme (see col. 8, line 42-67, col. 10, line 26-36) and the is RNA-DNA hybrid (see column 7,line 13-22). However, Impraim et al. did not teach blocker probe, immobilization of the probes and use of bridge probes or dT-tailed probes.

Natan et al teach a method of detecting a target nucleic acid comprising:

(a) hybridizing a target nucleic acid sample (DNA or RNA) (see column 2, lines 56-57) to a capture sequence probe (first oligonucleotide) and a signal sequence probe (second oligonucleotide probe) to form a double-stranded hybrids between said probes and the target nucleic acid, (b) adding a blocker to the hybridization reaction, where in said blocker hybridizes to excess non-hybridized capture probe sequences or signal probe sequences (see column 5, lines 31-63, column 21, lines 7-24). Natan et al. also teach that the method comprises formation of RNA-DNA hybrid (see column 6,lines 20-23).

Shah et al. teach a method of detecting a target nucleic acid wherein Shah et al. disclose that the method comprises hybridizing a target nucleic acid (DNA or RNA) to a capture probe and a detector probe (signal probe), and detecting the bound hybrid (see column 7, lines 17-29, column 3, lines 60-67, column 4, lines 1-51, and column 6, lines 30-57). Shah et al. also teaches immobilization of capture probe on to a solid support (see column 4, lines 29-32); The capture or release using first and second capture probes can be performed in either order (simultaneously or

sequentially) (see column 6, lines 58-65). Further Shah et al. teach use of dA-tailed probes (bridge probes) which bind to both target and dT derivitized supports such that the binding is stronger to the targets than the supports (see column 8, lines 44-54); capture probes biotinylated at both ends (column 9, lines 58-67); the capture probe and the detector probe distance when hybridized to a target comprises less than 3.0kb (see column 9. lines 31-57, see base pair distance of SEQ ID nos.1-4).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of detecting a target nucleic acid as taught by Impraim et al. with the step of adding blocker probes or oligonucleotides as taught by Nathan et al. and dT-tailed probes and immobilization of capture probes as taught by Shah et al. to achieve expected benefit of developing an enhanced and improved method for detecting a nucleic acid because Nathan et al. taught that use of blocker oligonucleotides reduces background signal (see col. 5, line 31-63) and Shah et al. taught that 'the new assay format eliminates noise due to nonspecific binding of the detector probe to the capture probe and can produce a sandwich hybridization assay entirely free of background noise (see col. 3, line 49-64). In order to reduce signal to noise ratio in hybridization assays involving DNA-RNA interaction, an ordinary practitioner would have been motivated to modify the method of detecting a target nucleic acid as taught by Imprain et al. by incorporating the steps of adding blocker oligonucleotides, immobilizing the capture probes and using dT-tailed probes as taught by Nathan et al. and Shah et al., to develop a method that would improve sensitivity and specificity of detecting a target nucleic acid which would result in reduced background signal noise and enhanced sensitivity and specificity of the detection method.

***Response to arguments***:

With regard to the above rejection Applicants' arguments are fully reviewed and found unpersuasive. Applicants argue that the instant claims are nonobvious over Impraim et al. in view of Nathan et al. and further in view of Shah et al. Applicants arguments are based on attacking each reference independently. According to MPEP 2145 One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants argue that Impraim et al. does not teach capture probe sequence and signal probe sequence. These arguments are found unpersuasive because Impraim et al. does teach RNA probes which are linked to detectable labels (see col. 6, line 34-47) in plurality that are considered as comprising capture and signal probes. Since the instant claims do not recite any structural limitations of (specific sequence) of capture and signal probes, the RNA probes of Impriam et al. comprise both capture and signal sequences and the broader scope of the instant claims do not exclude the limitations of Imprim et al.

Applicants further argue that Nathan et al. does not teach blocker probes having identical sequence to the target nucleic acid, rather teaches blocker probes having a complementary sequence to the capture probe and refers to the Fig. 2 of the instant specification. Examiner notes that "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims". In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant context, Applicants' arguments are fully considered and found unpersuasive because the blocker probe sequence complementary to a capture probe indicates

that the blocker probe comprise a sequence identical to the target sequence, the structural limitation of the blocker probe, upon which the arguments are based, is not present in the instant claims and the specification can not be read into the claims.

Applicants also argue that the Shah et al. does not teach bridge probes as claimed in the instant invention. These arguments are found unpersuasive since the instant claims do not recite any structural limitations of bridge probes, the broader scope of the instant claims do not exclude the limitations of Shah et al. Applicants further argue that there is no motivation or suggestion in any of the cited references either alone or in combination and the combination of the cited prior art does not make the claimed invention obvious. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992). In this case, specific motivation is provided in the rejection above, and an ordinary practitioner would be motivated to modify the method of detecting a target nucleic acid as taught by Imprain et al. by incorporating the steps of adding blocker oligonucleotides, immobilizing the capture probes and using dT-tailed probes as taught by Nathan et al. and Shah et al., to develop a method that would improve sensitivity and specificity of detecting a target nucleic acid which would result in reduced background signal noise and enhanced sensitivity and specificity of the detection method.

***Conclusion***

No claims are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

JEFFREY FREDMAN
PRIMARY EXAMINER
4/17/07

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Examiner
Art Unit 1637